PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P208356PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/NL2004/000748	International filing date *(day/month/year)* 25.10.2004	Priority date *(day/month/year)* 24.10.2003
International Patent Classification (IPC) or national classification and IPC A23L1/29, A23L1/30, A61K31/733, A61K31/702, A61K35/74, A61P37/00		
Applicant N.V. NUTRICIA et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet..
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23.08.2005	15.12.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Barnas, C Telephone No. +49 89 2399-7469

Form PCT/IPEA/409 (Cover Sheet) (January 2004)

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NL2004/000748

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements* of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-34 as published

Sequence listings part of the description, Pages

1-8 received on 03.01.2005 with letter of 03.01.2005

Claims, Numbers

1-18 received on 23.08.2005 with letter of 22.08.2005

Drawings, Sheets

1, 2 as published

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* If item 4 applies, some or all of these sheets may be marked "superseded."

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-18
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☒ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☒ received by this Authority as an amendment on

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The documents mentioned in the present International Preliminary Report are numbered as in the International Search Report. D1 corresponds to the first document of the Search Report, D2 to the second document etc.

Art. 33(3) PCT

D2 discloses mixtures of at least two non-digestible soluble carbohydrate components having a different structure and differing in the average length by at least 5 monosaccharides. The problem to be solved is the provision of a carbohydrate mixture for improving the intestinal flora. The problem is solved by providing a preparation as described in claim 1 which, in addition, comprises Bifidobacterium breve. The cited prior art does not contain any hint that would prompt the skilled person to provide such a preparation. Claims 1-17 are therefore inventive. The cited prior art does also not contain any hint that would prompt the skilled person to use a mixture as described in claim 18 for the manufacture of a composition for decreasing the relative amounts of the indicated bacteria. Said claim is therefore also inventive.

Re Item VIII

Certain observations on the international application

Art. 6 PCT

The wording of claim 4 ("... wherein the carbohydrate components comprises 95 to 60 wt% and the carbohydrate B comprises 5 to 40 wt% with A + B = 100%.") cannot be understood from the technical point of view. Said claim is therefore not clear, contrary to Art. 6 PCT. In view of the description of the present application said claim has been examined as "... wherein the carbohydrate component A comprises 95 to 60 wt% and the carbohydrate B comprises 5 to 40 wt% with A + B = 100%."

Amended claims

1. A preparation comprising *Bifidobacterium breve* and a mixture of at least two non-digestible soluble carbohydrate components A and B, wherein
- said carbohydrate component A has a different structure from said carbohydrate component B;
- said carbohydrate component A is present in an amount of 5 to 95 % by weight of the sum of carbohydrate components A and B;
- at least 50% of the total non-digestible soluble carbohydrates is selected from disaccharides to eicosasaccharides; and
- carbohydrate components A and B differ in the (average) number of monosaccharide units, carbohydrate component A having an average chain length which is at least 5 monosaccharide units lower than the average chain length of component B.

2. A preparation according to claim 1, wherein said carbohydrate components A and B differ in the structure of the monosaccharide units of the carbohydrate.

3. A preparation according to claim 1 or 2, wherein said carbohydrate component A is selected from indigestible monosaccharides up to hexasaccharides of the same carbohydrate structure, and said carbohydrate component B is selected from indigestible heptasaccharides and higher polysaccharides of the same carbohydrate structure.

4. A preparation according to any one of claims 1-3, wherein the carbohydrate components comprises 95 to 60 wt% and the carbohydrate B comprises 5 to 40 wt%, with A + B = 100 wt%.

5. A preparation according to any one of claims 1-4, wherein at least 60 wt%, preferably 80 to 100 wt% of said carbohydrate component A belong to the group of galacto-oligosaccharides, preferably to the group of trans-galacto-oligosaccharides.

6. A preparation according to any one of claims 1-5, wherein at least 60 wt%, preferably 80 to 100 wt% of said carbohydrate component B belong to the group of fructo-polysaccharides, including inulin.

7. A preparation according to any one of claims 1-6, comprising 10^5 to 10^{11} cfu of *Bifidobacterium breve* per g of total non-digestible soluble carbohydrate.

8. A preparation according to any one of claims 1-7 for use as a supplement, wherein the probiotic *Bifidobacterium breve* is present in the supplement in an amount of $1x10^5$ to $1.5x10^{11}$ cfu/g, calculated on the basis of the supplement.

9. A preparation according to any one of claims 1-7 for use as an infant nutrition, wherein the *Bifidobacterium breve* is present in the supplement in an amount of $1x10^2$ to $1x10^{12}$ cfu/g of the infant supplement.

10. An infant nutrition supplement comprising a preparation according to any one of claims 1-8, and further comprising digestible carbohydrate, a lipid source, or a protein source, or a mixture thereof.

11. An infant nutrition comprising a preparation according to any one of claims 1-7 and 9, and further comprising digestible carbohydrate, a lipid source, and a protein source.

12. Use of a preparation according to any one of claims 1-9 for the manufacture of a composition for the normalisation of the *Bifidobacterium* species composition in the gastro-intestinal tract of non- or partially breast-fed infants to the composition in breast-fed infants.

13. Use of a preparation according to any one of claims 1-9 for the manufacture of a composition for the prevention or treatment of one or more immune disorders.

14. Use according to claim 13, wherein said immune disorders are selected from allergy, atopy, allergic rhinitis, food hypersensitivity, atopic dermatitis, eczema and asthma.

15. Use according to claim 13 or 14, wherein said immune disorders are selected from diarrhoea and viral diarrhoea.

16. Use of a preparation according to any one of claims 1-9 for the manufacture of a composition for preventing and/or treating energy malabsorption.

17. Use of a preparation according to any one of claims 1-9 for the manufacture of a composition for inhibiting the infiltration of eosinophils, neutrophils and mononuclear cells in allergic lesions, inhibiting the Th2 type immune response and/or stimulating the Th1 mediated immune response.

18. Use of a mixture of at least two non-digestible soluble carbohydrate components A and B, wherein

- said carbohydrate component A is present in an amount of from 5 to 95 % by weight of the sum of carbohydrate components A and B;
- at least 50% of the total non-digestible soluble carbohydrates is selected from disaccharides to eicosasaccharides; and
- said carbohydrate components A and B differ (i) in the (average) number of monosaccharide units of the carbohydrate, (ii) in the structure of the monosaccharide units of the carbohydrate, or (iii) both,

for the manufacture of a composition for decreasing the relative amounts of *Bifidobacterium catenulatum*, *B. pseudocatenulatum* and/or *B. adolescentis* in the gastro-intestinal tract of non- or partially breast-fed infants.